

Short reports

Chronic necrotising pulmonary aspergillosis caused by *Aspergillus niger* in a mildly immunocompromised host

M Yamaguchi, H Nishiya, K Mano, O Kunii, H Miyashita

Abstract

A middle aged man with diabetes mellitus and chronic alcoholic hepatitis developed chronic necrotising pulmonary aspergillosis or semi-invasive aspergillosis due to *Aspergillus niger*.

Semi-invasive pulmonary aspergillosis occurs in patients with mild systemic immunosuppression and is defined as an indolent, cavitating process due to invasion of lung tissue by fungi of the *Aspergillus* genus.¹ *A. fumigatus* is the most common organism concerned. We describe a fatal case of chronic necrotising pulmonary aspergillosis caused by *A. niger*.

Case report

A 54 year old man with diabetes mellitus and chronic alcoholic hepatitis gave a three month history of fever, haemoptysis, weight loss, and increasing shortness of breath. His diabetes was previously well controlled with insulin. He had a pancreatoduodenectomy for pancreatolithiasis and stenosis of the common bile duct in 1986. On admission he was poorly nourished and febrile (40°C). A chest radiograph showed non-cavitating pneumonia in the right upper lobe. The white blood cell count was $8.3 \times 10^9/l$ with 72% neutrophils, glutamic oxaloacetic transaminase activity was 154 U/l, glutamic pyruvic transaminase 63 U/l, lactate dehydrogenase 710 U/l, γ glutamyl transpeptidase 1048 U/l, and the serum glucose concentration 13.66 mmol/l. Treatment with amikacin sulphate and clindamycin was started. Sputum culture grew *Enterobacter cloacae*, *Klebsiella oxitoca* and *Haemophilus parainfluenzae*. Fibreoptic bronchoscopy showed erosive bronchitis and culture of washings and brushings yielded *Acinetobacter* sp and *Candida albicans*.

Despite antibiotic treatment his conditions slowly deteriorated and his diabetes became difficult to control. After two weeks' treatment a repeat chest radiograph showed right upper

lobe consolidation with pleural thickening and infiltrates in the middle lobe (fig 1) and he was transferred to our department.

On examination he was not cyanosed but remained febrile (38.2°C). His respiratory rate was 24/min and pulse rate 102/min. Coarse inspiratory crackles were heard over the right upper and middle lung fields. He was anaemic (haemoglobin 7.2 g/dl) and his white blood cell count was $31.5 \times 10^9/l$ with 93% neutrophils. The serum total protein concentration was 49 g/l, urea 2.3 mmol/l, creatinine 53.04 μ mol/l, and glucose 24.98 mmol/l. Sputum culture yielded *Candida glabrata* and *Enterobacter cloacae*. Culture of a transtracheal aspirate grew *Candida*. His treatment was changed to carbapenem with fluconazole 200 mg/day and amphotericin B in doses increasing to 45 mg/day. He remained febrile and the chest radiograph continued to show extensive infiltration. Antituberculous drugs (rifampicin and isoniazid) were added to his treatment. On his 19th day in hospital he developed disseminated intravascular coagulation with acute renal failure and severe respiratory failure, and died after 22 days in hospital.

At postmortem examination there was a turbid yellow pleural effusion (460 ml) on the right side. The right lung was extremely heavy (1250 g). A 10 cm area of massive necrosis without an apparent cavity and with dark brown pigmentation occupied most of the right upper lobe; there was evidence of severe bronchopneumonia with purulent mucus in the bronchi in the middle and lower lobe (fig 2A). Microscopy of the necrotic lung tissue showed infiltration with *Aspergillus* hyphae, but no *Candida*. The fungus was confirmed to be *Aspergillus niger* by the characteristic morphological features of globose vesicles with radiate phialide (fig 2B). Postmortem culture of the lung yielded no fungus. A moderate amount



Figure 1 Chest radiograph showing consolidation in the right upper and middle lobes.

Second Department of Medicine, Teikyo University School of Medicine, Itabashi-Ku, Tokyo 173, Japan

M Yamaguchi
H Nishiya
K Mano
O Kunii
H Miyashita

Reprint requests to:
Dr M Yamaguchi

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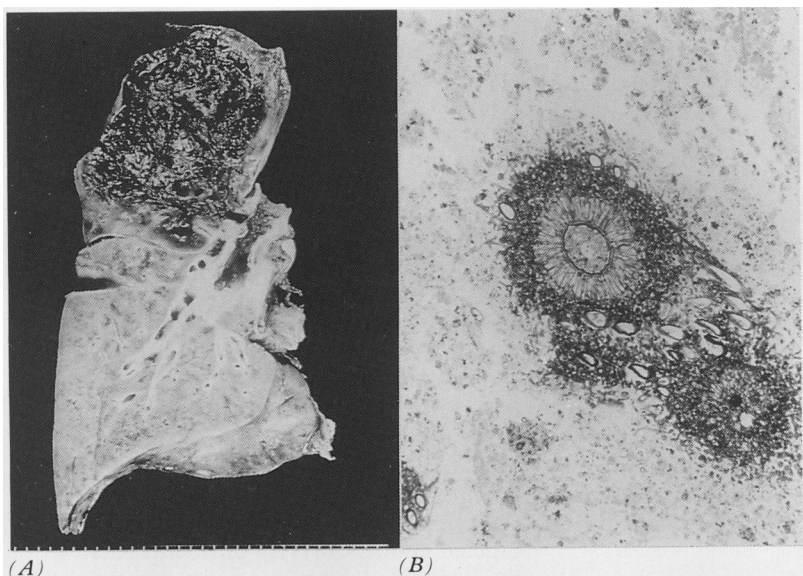


Figure 2 A—Massive necrosis with dark brown pigmentation in the right upper lobe without apparent cavity formation. B—Characteristic hyphae of *Aspergillus niger* showing a globose vesicle and radiate phialide. (Grocott methenamine silver stain.)

of calcium oxalate crystal had been deposited in the necrotic lung tissue. Thrombosis in the pulmonary artery was due to *A. niger*, but no evidence of disseminated aspergillosis was found.

Discussion

Pulmonary aspergillosis is generally classified into allergic bronchopulmonary aspergillosis, aspergilloma (fungus ball), and invasive pulmonary aspergillosis. The latter includes acute invasive pulmonary aspergillosis and chronic necrotising pulmonary aspergillosis. Acute invasive aspergillosis is a fulminant pneumonia often with dissemination, which usually occurs in severely immunocompromised patients. The chronic disorder is slowly progressive with pulmonary infiltrates and often a newly formed cavity, which frequently contains a ball of heavily infected necrotic lung tissue. It usually develops in states of mild systemic immunosuppression, such as connective tissue disorders, poor nutrition, diabetes mellitus, and long term low dose corticosteroid treatment. Most patients with semi-invasive aspergillosis have a white blood cell count greater than $10 \times 10^9/l$, whereas patients with invasive aspergillosis are usually granulocytopenic.¹

Our patient had predisposing factors: poor nutrition, diabetes mellitus, previous surgery,

and chronic alcoholic hepatitis. Poor control of his diabetes may have depressed the phagocytic function of the polymorphonuclear leucocytes,² which may have predisposed him to bronchopneumonia, leading to aspergillus infection. A large alcohol intake may also reduce pulmonary alveolar macrophage function³ and allow invasion by aspergillus.

The lesion was almost confined to the right upper lobe, with pleural thickening but no cavity formation. In chronic necrotising pulmonary aspergillosis mycetomas form in cavities resulting from tissue necrosis and invasion by the fungus.¹ In our patient the aspergillus infection was only slowly progressive but bacterial bronchopneumonia and acute renal failure led to his death. This case was probably an early stage of local invasive disease occurring in a mildly immunocompromised patient.

The most common organism causing chronic necrotising pulmonary aspergillosis is *A. fumigatus*, though there are three reports of cases caused by *A. niger*.^{1,4} *A. niger* may produce calcium oxalate crystals,⁴ as found in our case, and their presence is highly suggestive of *A. niger* infection.⁵ Although sputum cultures did not yield *A. niger* in this case, microscopic examination of lung tissue showed characteristic vesicles and phialide of *A. niger*, which are unique enough to distinguish *A. niger* from other *Aspergillus* species. *Candida* species were isolated from tracheal aspirates in our patient and this association has been noted before.⁴

We chose fluconazole to treat the candida infection and it probably was effective because no candida was found in necrotic lung tissue at necropsy. The treatment of choice for aspergillus infection is a combination of amphotericin B and flucytosine, which was unsuccessful in our case.

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